in line 3, after "(HIV)" insert --antigen-- ; and

in line 3, delete "and Feline Immunodeficiency Virus (FIV)".

In claim 24, line 2, delete "or FIV".

In claim 28, line 2, delete "or Feline Immunodeficiency Virus (FIV) antigen"; and

in line 3, delete "or FIV".

REMARKS

By this Amendment, Applicants have canceled claims 21, 22, 25, 26, 27, and 32 without prejudice or disclaimer and have amended claims 19, 24, and 28. Claims 19, 20, 23, 24, 28, 29, 30, and 31 are pending in this application.

The Examiner has maintained the rejection of claims 19-32 under 35 U.S.C. § 112, first paragraph, for the reasons stated in the Office Actions of November 24, 1997 and August 10, 1998. In responding to Applicants' arguments and the declaration of Dr. Voss of May 22, 1998, the Examiner makes five specific points regarding Applicants' position.

In point (a), the Examiner states that the declaration of Dr. Voss does not address FIV antigens or vaccines. Applicants have obviated this point by canceling claims directed to FIV and amending other claims to delete reference to FIV.

In point (d), the Examiner argues that the Voss declaration does not establish a synergistic response in the generation of gamma interferon when the adjuvants are

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used in conjunction with an antigen. Applicants have obviated this point by canceling the claims directed to generation of gamma interferon.

The Examiner takes the position in point (e) that the Voss declaration does not establish the fact that T-cell responses were generated to HIV or FIV, and it does not establish the identity of cell type involved. Applicants have obviated this point as well by canceling claims directed to stimulating T-cell responses.

In points (b) and (c), the Examiner states that the Voss declaration does not demonstrate the following: the ability of CTL responses to reduce viral burden or load; that CTL responses generated after vaccination provide protection; or a correlation between HIV-specific CTL responses and the slowing of progression to AIDS.

Applicants take this opportunity to provide a second declaration from Dr. Voss dated January 15, 1999 and an article by Mooij et al., *A Clinically Relevant HIV-1 Subunit Vaccine Protects Rhesus Macaques From In Vivo Passaged Simian-Human Immunodeficiency Virus Infection*, AIDS (Fast Track), 12:F15-F22 (1998) which demonstrated that the invention is enabling to one of ordinary skill in the art. In paragraph 6 of the enclosed Voss declaration, Dr. Voss provides a foundation for the experimental results of the Mooij et al. article. Dr. Voss explains that a standard method of measuring the ameliorative effects of a therapeutic strategy is to measure viral burden or viral load. When animals are protected from infection, there is no detectable viral burden or viral load. Furthermore, protected vaccines, because they show no viral load or burden, do not progress to AIDS.

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In paragraph 7 of the declaration, Dr. Voss states that in the Rhesus monkey SHIV model, a model Applicants established in the Response of May 22, 1998 to be an accepted HIV model, two of four monkeys vaccinated with vaccines containing the claimed QS21 and 3D-MPL adjuvants were protected from infection. Thus, in the two protected monkeys, there was no viral burden or viral load. This protection from infection was observed despite a lack of interpretable CTL data. Furthermore, in the two monkeys that were not protected from ultimate infection, HIV Polymerase Chain Reaction (PCR) testing revealed a reduced virus isolation (Quantitative Virus Isolation (QVI)) in comparison to the control group of animals that were not vaccinated. Voss Declaration, paragraph 8. The results of these experiments are documented in Mooij et al.

Mooij et al. expanded the Rhesus monkey test to include an additional vaccination of four monkeys with an emulsion of the claimed adjuvants and gp120. It is important to note that the claimed invention includes oil-in-water emulsions of adjuvants (col. 5, line 38). All of the four Rhesus monkeys challenged in Group B "remained completely virus-free in PBMC at all time-points tested after challenge." Mooij et al., p. F19. A third group of monkeys, Group C, was initially immunized with an inferior unrelated adjuvant that generated only a very weak immune response. The Group C monkeys were later immunized with the claimed adjuvant in order to "determine whether the SBAS2 adjuvant formulation [an oil-in-water emulsion of the claimed adjuvants] was capable of improving previously weak immune responses, and if so, to

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see whether protective immunity could be achieved." Mooij et al., p. F16. As in the Group B monkeys, all Group C vaccines were completely virus-free at all times tested after challenge. Mooij et al., p. F19; Voss Declaration, paragraph 11. In other words, out of twelve animals vaccinated, ten were conclusively protected from infection.

It is not the Applicants' duty to explain the scientific principles behind their invention. *E.g., Fromson v. Advance Offset Plate, Inc.*, 219 U.S.P.Q. 1137, 1140 (Fed. Cir. 1983) ("[I]t is axiomatic that an inventor need not comprehend the scientific principles on which the practical effectiveness of his invention rests."). Applicants have removed from examination claims related to the stimulation of CTL response and IFN-γ production. Applicants' claims are now directed to vaccine compositions, processes for making vaccine compositions, and methods for enhancing the immune response by administering the claimed vaccine composition. The amended claims do not recite an explicit mechanism for defeating HIV; rather, they, along with the rest of the specification, teach "how to achieve the claimed result[s]" listed *supra*. *Newman v. Quigg*, 11 U.S.P.Q.2d 1340, 1345 (Fed. Cir. 1989). Accordingly, the application is now in condition for immediate allowance and the Applicants respectfully request the Examiner to immediately allow the claims.

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If there is any additional fee for this Amendment, including a fee for an extension of time, please charge any such fee to Deposit Account No. 06-916.

Respectfully submitted,

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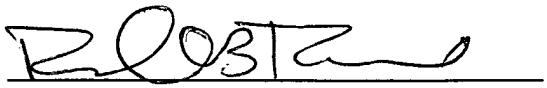
By: 

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